

choosing among resources spent on new drugs and on the number of nurses at night in geriatric wards or on facilities in the community for people with learning disabilities. Rationing in Britain works mostly by dilution rather than denial: it's politically so much easier, particularly if you dilute services for the most marginal.

NICE will be concerned with what's already there through its work on guidelines, and Sir Michael has a vision that "doctors will go to work with the *British National Formulary* in one pocket and a copy of NICE guidelines in the other."⁴ Sadly, this vision may reflect Sir Michael's naivety about guidelines. Firstly, guidelines that covered every eventuality would be carried in a wheelbarrow not a pocket. Secondly, guidelines are difficult and expensive to produce, and the most tricky part is making the jump from evidence to recommended actions. Those making that jump resort not only to wisdom but also to prejudice and self interest. Thirdly, guidelines on their own change nothing.⁵

Here we arrive at what may be the biggest failing of NICE. Centralist direction is a poor way of solving the NHS's biggest problem, the fact that good practice may flourish in one clinic and fail to spread even to the clinic next door let alone the rest of the NHS. Meanwhile, poor practice gaily continues. Those who try to run the NHS are understandably frustrated by these failures and naturally turn to organisations like NICE and its less often mentioned brother CHI (Commission for Health Improvement, or "nasty" as it's widely known) to put things right. But their controlling instincts are probably wrong. "Over the long run," writes Peter Senge, an academic at the Massachusetts Institute of Technology and one of the originators of the idea of the learning organisation, "superior

performance depends on superior learning."⁶ And control limits learning. "Control limits space. Learning needs space," said Arie de Geus, probably the originator of the learning organisation.⁷ "It is simply no longer possible for anyone to 'figure it all out at the top' "⁶ and "little significant change can occur if it is driven from the top."⁸ Ironically, both Senge and de Geus were speaking at a symposium organised to identify how to sustain the NHS for the next 50 years.

In conclusion, NICE should help with rationalising the introduction of new technologies into the NHS, and the less politicised and more transparent its process the better. It might develop into an effective means of rationing all health care, but it is likely to struggle with solving the important problem of variable performance throughout the NHS. No one institution could produce so much.

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*NICE covers only the English and Welsh NHS; in Scotland similar functions will be performed by the Clinical Resource and Audit Group and the Clinical Standards Board; and Northern Ireland is still consulting about its structures.

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The evidence for β blockers in heart failure

Equals or surpasses that for angiotensin converting enzyme inhibitors

Heart failure is a common, malignant condition for which hospital admissions are rising rapidly.¹⁻³ Despite the evidence that angiotensin converting enzyme inhibitors improve the morbidity and mortality of heart failure secondary to left ventricular systolic dysfunction, the prognosis of heart failure in the community has improved little over the past 30 years.⁴ This may reflect a reluctance to prescribe angiotensin converting enzyme inhibitors.⁴ Now, however, evidence has accumulated to show that β blockers, when used in addition to angiotensin converting enzyme inhibitors, also reduce mortality in heart failure. Will this be another lost opportunity?

The CIBIS-II study,⁵ comparing bisoprolol with placebo, recently reported a highly significant reduction in all cause mortality. When these data and those from other smaller trials⁶⁻⁸ identified from searches of Medline and Embase and recent meetings⁹ are added to those reported in previous meta-analyses¹⁰ there are now 25 trials that have randomised patients with heart failure to β blocker or control, comprising 6511 patients and 810 deaths. Overall β blockers reduced

the odds of death by 36% (95% confidence interval 25% to 45%) (fig 1). There is no evidence of heterogeneity between the trial results ($Q=12.7$; $df=24$; $P=0.97$) and no evidence of publication bias. Also, the MERIT trial, which randomised 3991 patients, was recently stopped because of a large treatment effect (provisionally a 35% reduction), lending further support for the benefits of β blockade. By comparison angiotensin converting enzyme inhibitors were associated with a 24% (13% to 33%) reduction in the odds of

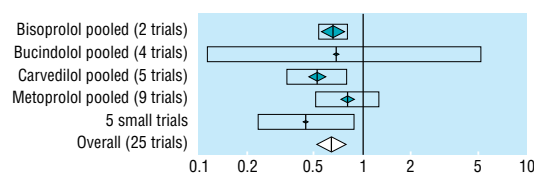


Fig 1 Pooled odds ratios (and 95% confidence intervals) describing the effect of β blockers on mortality in patients with heart failure (fixed effects model¹¹)

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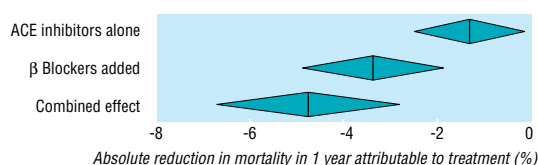


Fig 2 Effect on annual rate of mortality (%) of angiotensin inhibitors alone, with β blockers added, and with both drugs. Risk differences and 95% confidence intervals estimated by method of Ioannidis et al¹³

death in the 39 trials in patients with heart failure (8308 patients and 1361 deaths).¹²

β Blockers have an effect as great as or greater than that of angiotensin converting enzyme inhibitors. However, most patients in trials of β blockers were already taking angiotensin converting enzyme inhibitors, so the benefits of β blockade appear additional to those of angiotensin converting enzyme inhibitors. Fig 2 describes (a) the reduction in annual mortality achieved by angiotensin converting enzyme inhibitors, (b) the reduction achieved by β blockers among patients largely treated with angiotensin converting enzyme inhibitors, and (c) the best available estimate for the effect of the combination. Although this estimate must be treated with caution, because it combines data from different groups of trials, the annual rate of mortality is similar among the active treatment groups in the 39 angiotensin converting enzyme inhibitor trials (10%) and in the control groups in the 25 β blocker trials (12%), suggesting that summing the benefits is reasonable.

The number of patients with heart failure who have to be treated for one year to prevent one death is 74 for angiotensin converting enzyme inhibitors, 29 when a β blocker is added to an angiotensin converting enzyme inhibitor, and 21 for the combined use of both types of drug. The evidence that β blockers reduce mortality in patients with heart failure due to left ventricular systolic dysfunction is now compelling.

What are the implications for clinical practice? Some large subgroups of patients with heart failure—such as those aged over 75—are poorly represented in the trials, and more evidence of benefit is required for both classes of agents in older patients. Only carvedilol is licensed for use in heart failure at present, and it cannot be assumed that all β blockers are equally effective. A large mortality study is currently comparing metoprolol to carvedilol in patients with heart failure.

Experience is required to use β blockers safely in heart failure, and initially many practitioners will want to use the expertise of their local cardiologist. The first aim must be to identify those patients whose heart failure is caused by left ventricular systolic dysfunction. This will usually require echocardiography. Angiotensin converting enzyme inhibitors and β blockers are not of proved benefit for patients with heart failure due to other causes.

The second aim should be to include β blockers as part of a strategy of preventing heart failure.^{3,4} Unlike angiotensin converting enzyme inhibitors and diuretics, β blockers are of limited use, and may be dangerous, as “rescue” treatment in crises such as pulmonary oedema or other conditions that confine the patient to bed. They are most effectively and safely used

in patients with milder symptoms to retard deterioration and increase the length and quality of life.

The third important point is that, like angiotensin converting enzyme inhibitors, β blockers need to be started in low doses. Unlike them, however, β blockers require slow titration over weeks or months before patients can attain maintenance doses: start low and go slow.

Realising the benefits of this effective and inexpensive treatment requires a reorganisation of services for managing heart failure, for it appears that the current system has failed to deliver effective and efficient care. Several structures are being advocated, including heart failure clinics and liaison nurses. The health service has tried to ignore heart failure as a problem for far too long. Now that one in 20 medical beds (and rising) is occupied by a patient with heart failure it must be clear that ignoring the problem is not a sensible option.

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JGFC has spoken at many meetings and educational programmes on drugs in heart failure organised by pharmaceutical and device companies and received fees. He has also received research funding from industry as well as the NHS, British Heart Foundation, and US Veterans Administration. JGFC and NF received an unrestricted grant from SmithKline Beecham to produce an updated meta-analysis of β blockers after myocardial infarction. JMcG is currently funded by SmithKline Beecham, who supply carvedilol in the US.

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